



BILLING CODE 6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2012-0919; FRL-9946-30]

Halauxifen-methyl; Pesticide Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes tolerances for residues of halauxifen-methyl and its metabolite, XDE-729 acid, in or on multiple commodities which are identified and discussed later in this document. Dow AgroSciences LLC requested these tolerances under the Federal Food, Drug, and Cosmetic Act (FFDCA).

DATES: This regulation is effective [*insert date of publication in the Federal Register*].

Objections and requests for hearings must be received on or before [*insert date 60 days after date of publication in the Federal Register*], and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2012-0919, is available at <http://www.regulations.gov> or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703)

305-5805. Please review the visitor instructions and additional information about the docket available at <http://www.epa.gov/dockets>.

FOR FURTHER INFORMATION CONTACT: Susan Lewis, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (703) 305-7090; email address: RDFRNotices@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How Can I Get Electronic Access to Other Related Information?

You may access a frequently updated electronic version of EPA's tolerance regulations at 40 CFR part 180 through the Government Printing Office's e-CFR site at http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.

C. How Can I File an Objection or Hearing Request?

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2012-0919 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before *[insert date 60 days after date of publication in the **Federal Register**]*. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA-HQ-OPP-2012-0919, by one of the following methods:

- *Federal eRulemaking Portal:* <http://www.regulations.gov>. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.

- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at <http://www.epa.gov/dockets/contacts.html>. Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at <http://www.epa.gov/dockets>.

II. Summary of Petitioned-For Tolerance

In the **Federal Register** of February 15, 2013 (78 FR 11126) (FRL-9378-4), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 2F8086) by Dow AgroSciences, 9330 Zionsville Road, Indianapolis, IN 46268. The petition requested that 40 CFR part 180 be amended by establishing tolerances for residues of the herbicide, halauxifen-methyl (methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate) and its major metabolite, XDE-729 acid, expressed as halauxifen-methyl (parent) equivalents, in or on barley, grain at 0.01 parts per million (ppm); barley, hay at 0.01 ppm; barley, straw at 0.01 ppm; cattle, fat at 0.01 ppm; cattle, meat at 0.01 ppm; cattle, meat byproducts at 0.01 ppm; goat, fat at 0.01 ppm; goat, meat at 0.01 ppm; goat, meat byproducts at 0.01 ppm; horse, fat at 0.01 ppm; horse, meat at 0.01 ppm; horse, meat byproducts at 0.01 ppm; milk at 0.01 ppm; sheep, fat at 0.01 ppm; sheep, meat at 0.01 ppm; sheep, meat byproducts at 0.01 ppm; wheat, forage at 0.5 ppm; wheat, grain at 0.01 ppm; wheat, hay at 0.04 ppm; and wheat, straw at 0.015 ppm. That document referenced a summary of the petition prepared by Dow AgroSciences LLC, the registrant, which is available in the docket, <http://www.regulations.gov>. There were no comments received in response to the notice of filing.

Based upon review of the data supporting the petition, EPA has determined that livestock commodity tolerances are not required for the proposed uses. In addition, the proposed “wheat, hay” tolerance level of 0.04 ppm will be set at a reduced tolerance level of 0.03 ppm. The reason for these changes are explained in Unit IV.C.

III. Aggregate Risk Assessment and Determination of Safety

Section 408(b)(2)(A)(i) of FFDCA allows EPA to establish a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is “safe.” Section 408(b)(2)(A)(ii) of FFDCA defines “safe” to mean that “there is a reasonable certainty

that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.”

This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Section 408(b)(2)(C) of FFDCA requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to “ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue....”

Consistent with FFDCA section 408(b)(2)(D), and the factors specified in FFDCA section 408(b)(2)(D), EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure for halauxifen-methyl and its acid metabolite, including exposure resulting from the tolerances established by this action. EPA's assessment of exposures and risks associated with halauxifen-methyl and its major metabolite, XDE-729 acid, follows.

A. Toxicological Profile

EPA has evaluated the available toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

The toxicology database for halauxifen-methyl is considered adequate at this time. Following oral exposure and absorption, the liver is exposed pre-systemically to halauxifen-methyl, where it is hydrolyzed to its major metabolite, XDE-729 acid, before entering the systemic circulation. Therefore, systemic exposure to organs and tissues other than the liver is to XDE-729 acid, whereas the liver is also exposed to the parent prior to its metabolism. The

guideline studies were conducted on XDE-729 acid and identified the kidney as the main target organ. Bridging studies on halauxifen-methyl identified the liver as the target organ, but the data could not bridge to the acid metabolite because liver toxicity from exposure to halauxifen-methyl occurred at lower doses than the kidney toxicity resulting from exposure to XDE-729 acid. In *lieu* of conducting long-term oral studies on halauxifen-methyl, mechanistic studies were performed to characterize the mode of action (MOA) for liver toxicity. These studies identified activation of the liver aryl hydrocarbon receptor (AhR) as the MOA, and the molecular initiating event (MIE), for liver toxicity, for which increased liver Cyp1a1 gene expression serves as a biomarker. In the absence of this MIE, liver toxicity from parent halauxifen-methyl, including induction of hepatocellular proliferation, will not be observed. A point of departure (POD) of 3 mg/kg/day for increased Cyp1a1 expression (observed at 10 mg/kg/day, the study NOAEL) was identified in the rat 90-day dietary study on halauxifen-methyl and was selected for chronic dietary risk assessment, since it protects for the initial step in liver toxicity, regardless of exposure duration. Therefore, the bridging and mechanistic studies were considered along with the guideline studies in selection of the dose and endpoint for halauxifen-methyl. Based on the abundance of guideline and mechanistic data available, a MOA approach was used for the identification and characterization of hazard. Due to the distinct toxicities of the two compounds and the unique MOA for liver toxicity of halauxifen-methyl, risk from the two compounds was assessed separately.

There is no evidence of neurotoxicity or immunotoxicity for either compound. Inhalation studies (including the acute LD₅₀ study) were waived because MOEs for inhalation exposure, calculated using a highly conservative endpoint from oral data, were high ($\geq 2,500$), and the available oral and dermal studies did not indicate the potential for portal of entry effects. In addition, halauxifen-methyl has a low vapor pressure and adequate particle sizes for

test atmospheres could not be generated. Guideline rat or rabbit dermal toxicity, rat two-generation reproductive toxicity, dog chronic toxicity, rat chronic toxicity/carcinogenicity, mouse carcinogenicity, rat acute and subchronic neurotoxicity studies on halauxifen-methyl were also waived. The waivers were granted because adequate data were available for XDE-729 acid, to which systemic exposure would occur. The available data, when combined with the bridging and MOE data on halauxifen-methyl, allowed identification of a protective POD for AhR-mediated liver toxicity. Therefore, an additional database uncertainty factor (UF_{DB}) is not required for either compound. Both are mild eye irritants (Category III) but not dermal irritants or sensitizers. XDE-729 acid is classified as “not likely to be carcinogenic to humans.”

Halauxifen-methyl is classified as “not likely to be carcinogenic to humans at doses that do not induce Cyp1a1 expression,” based on the premise that AhR activation and subsequent promotion of hepatocellular tumors (via a prolonged increase in hepatocellular proliferation), a well-known non-genotoxic mechanism of liver carcinogenesis that has been previously described for other chemicals, depend upon this molecular initiating event (MIE). Moreover, based on its rapid metabolism to XDE-729 acid, halauxifen-methyl is not expected to persist in the body; therefore, progression of liver toxicity (including carcinogenic potential) from sustained AhR activation is not expected. Neither compound showed evidence of genotoxicity.

There is no evidence of increased prenatal susceptibility to either compound in developmental toxicity studies in two species. No developmental toxicity was observed in the presence of maternal toxicity for rats exposed to halauxifen-methyl or rabbits exposed to XDE-729 acid. In rats exposed to XDE-729 acid, mild fetal effects (decreased body weight and delayed ossification of the thoracic centra) were observed in the presence of more significant maternal toxicity (moribund sacrifice due to excessively decreased body weight and food consumption, along with increased relative kidney weight). In rabbits exposed to halauxifen-

methyl, the fetal effects (decreased body weight, increases in delayed ossification of the pubis) were observed in the presence of maternal liver histopathology and increased liver weight, at a dose greater than the maternal LOAEL, and were therefore not considered indicative of greater sensitivity. In a rat two-generation reproductive toxicity study on XDE-729 acid, there was no evidence of increased postnatal susceptibility. Parental toxicity in the rat two-generation reproductive toxicity study was observed at 443 mg/kg/day (NOAEL 103 mg/kg/day), but no offspring or reproductive toxicity was reported. A reproductive toxicity study was not conducted on halauxifen-methyl. Residual concerns for postnatal susceptibility to halauxifen-methyl in the absence of this study are low, due to selection of a highly conservative endpoint and assumptions for dietary exposure, as well as the low level of exposure expected from proposed use patterns.

Specific information on the studies received and the nature of the adverse effects caused by halauxifen-methyl and its metabolite, XDE-729 acid, as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies can be found at <http://www.regulations.gov> in document Halauxifen-methyl – New Active Ingredient Human Health Risk Assessment for Proposed Uses on Cereal Grains (Barley, Wheat, and Triticale) at page 42 in docket ID number EPA-HQ-OPP-2012-0919.

B. Toxicological Points of Departure/Levels of Concern

Once a pesticide's toxicological profile is determined, EPA identifies toxicological points of departure (POD) and levels of concern to use in evaluating the risk posed by human exposure to the pesticide. For hazards that have a threshold below which there is no appreciable risk, the toxicological POD is used as the basis for derivation of reference values for risk assessment. PODs are developed based on a careful analysis of the doses in each toxicological study to determine the dose at which no adverse effects are observed (the NOAEL) and the lowest dose

at which adverse effects of concern are identified (the LOAEL). Uncertainty/safety factors are used in conjunction with the POD to calculate a safe exposure level - generally referred to as a population-adjusted dose (PAD) or a reference dose (RfD) - and a safe margin of exposure (MOE). For non-threshold risks, the Agency assumes that any amount of exposure will lead to some degree of risk. Thus, the Agency estimates risk in terms of the probability of an occurrence of the adverse effect expected in a lifetime. For more information on the general principles EPA uses in risk characterization and a complete description of the risk assessment process, see <http://www.epa.gov/pesticides/factsheets/riskassess.htm>.

A summary of the toxicological endpoints for halauxifen-methyl used in the Agency's human health risk assessment is shown in Table 1(a) of this unit. No hazard from a single exposure was identified in the available database; therefore, no risk is expected from acute dietary exposure to halauxifen-methyl. For chronic dietary exposure, the rat 90-day oral study was selected. Although long-term oral toxicity studies are not available for halauxifen-methyl, a dose and an endpoint protective of long-term toxicity could be identified using the subchronic data together with the MOA data. The rat 90-day study NOAEL of 10.3 mg/kg/day was based on increased liver weight, hypertrophy and vacuolization consistent with fatty change at the LOAEL of 53.4 mg/kg/day. Liver effects at the LOAEL were of low severity but were considered treatment-related. A marked increase (1,500-fold above controls) in Cyp1a1 expression was also observed at the LOAEL. As previously noted, mechanistic studies on halauxifen-methyl identified activation of liver AhR as the MOA for liver toxicity, for which increased expression of Cyp1a1 in the liver is a biomarker for AhR activation, the MIE. In the absence of AhR activation, liver toxicity will not occur. Although there were no liver effects observed at the study NOAEL, a 52-fold increase in Cyp1a1 expression was observed. This increase is well below the increase that was associated with mild liver toxicity. Long-term effects on the liver from this lower level

increase are not known in the absence of chronic data, but the lowest dose in the study, 3 mg/kg/day, showed essentially no Cyp1a1 activation. Cyp1a1 expression at 3 mg/kg/day was comparable to controls in both the 28- and 90-day studies (1.2- and 3.6-fold higher than controls, respectively), indicating that there is not expected to be significant activation of the AhR receptor at this dose level over time. Therefore, in order to be protective of potential adverse effects on the liver following long-term exposure, the point of departure (POD) of 3 mg/kg/day was selected, based on increased expression of liver Cyp1a1 (52-fold) at 10 mg/kg/day. The selected dose and endpoint are considered conservative, since the dose is below the study NOAEL, but protective of residual uncertainty due to the lack of chronic data because liver toxicity may not occur in the absence of the MIE, regardless of exposure duration. They are also protective of chronic effects from XDE-729 acid, which are observed at higher doses. A UF of 100 is based on the combined interspecies (10x) and intraspecies (10x) UFs. An additional 10x UF for lack of chronic data was not applied for the following reasons: (1) progression of toxicity was not observed in the 28- and 90-day dietary studies in the rat: the NOAELs and LOAELs for both studies were the same, and the severity of the findings was minimal at both exposure durations; (2) evaluation of Cyp1a1 expression in the rat 28- and 90-day studies indicated that at the selected POD of 3 mg/kg/day, which is below the NOAELs for these studies, there is no expectation of significant AhR activation that could lead to liver toxicity. Observable liver toxicity in these studies was only associated with significantly greater levels of Cyp1a1; (3) halauxifen-methyl is rapidly metabolized to the acid, and neither bioaccumulate; and (4) based on comparative *in vitro* studies, humans are not anticipated to be more sensitive to liver effects of halauxifen-methyl than rats.

Carcinogenicity studies on halauxifen-methyl were not conducted. Systemic exposure from halauxifen-methyl is primarily to XDE-729 acid, which showed no evidence of

carcinogenicity. However, pre-systemic exposure of the liver to halauxifen-methyl was shown to activate the AhR receptor, an effect that induces an increase in hepatocellular proliferation and, subsequently, may promote an increased incidence of liver tumors with long-term exposure. The molecular marker for AhR activation, the MIE for liver toxicity, is increased expression of hepatic Cyp1a1, which was observed at a dose below the LOAEL for observable adverse effects of any type. The chronic dietary endpoint for halauxifen-methyl is based on the point of departure (POD) from the rat subchronic study for Cyp1a1 induction, as described above. The selected POD is considered very conservative because it is below the study NOAEL (the LOAEL was based on mild liver effects). Since Cyp1a1 induction is one of the early key events in the MOA leading to hepatotoxicity and promotion of hepatocellular proliferation, a dose that is protective of this event will be protective of the potential risk for liver cancer with chronic exposure, based on the rapid onset of AhR activation following initiation of exposure, and the lack of evidence of temporal progression of liver toxicity in the available studies (28- and 90-day). The MOA is considered relevant to human health risk assessment, but *in vitro* data suggest that humans are unlikely to be more sensitive than the rat. Based on a weight-of-the-evidence consideration, halauxifen-methyl is classified as “not likely to be carcinogenic to humans” at doses that do not induce liver Cyp1a1 expression.

Table 1(a).--Summary of Toxicological Doses and Endpoints for Halauxifen-methyl for Use in Human Health Risk Assessment

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects

Acute dietary (General population including infants and children and females age 13-49)	No hazard from a single exposure was identified in the available database; therefore, no risk is expected from this exposure scenario.		
Chronic dietary (All populations)	POD = 3.0 mg/kg/day $UF_A = 10x$ $UF_H = 10x$ FQPA SF = 1x	Chronic $RfD = 0.03$ mg/kg/day $cPAD = 0.03$ mg/kg/day	90-day oral toxicity in the rat (halauxifen-methyl) NOAEL = 10 mg/kg/day At the NOAEL, increased Cyp1a1 expression was observed (endpoint selected for risk assessment). The lowest dose of 3.0 mg/kg/day was selected to be protective of potential long-term effects from increased AhR expression in the liver. ¹ LOAEL = 52 mg/kg/day based on mild liver enlargement and pathology
Cancer (Oral, dermal, inhalation)	Classification: Not likely to be carcinogenic to humans at dose levels that do not induce Cyp1a1 expression. The cRfD is considered protective of potential cancer effects because it protects for the MIE for hepatocellular proliferation (AhR activation) that, over time, may result in promotion of liver tumors.		

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MIE = molecular initiating event

1. The POD selected for risk assessment was based on a non-adverse finding, increased liver Cyp1a1 expression in a rat 90-day dietary study, which was observed below the study NOAEL of 10 mg/kg/day for liver toxicity. This effect is a biomarker for activation of AhR, which causes liver toxicity and hepatocellular proliferation. The POD was selected to be protective of potential liver effects resulting from chronic dietary exposure to halauxifen-methyl. Other tissues and

organs will not be exposed to halauxifen-methyl due to rapid conversion to XDE-729 acid. The POD is protective of effects from exposure to XDE-729 acid.

A summary of the toxicological endpoints for XDE-729 acid used for human risk assessment is shown in Table 1(b) of this unit. No hazard from a single exposure was identified in the available database; therefore, no risk is expected from acute dietary exposure to XDE-729 acid. The chronic toxicity/carcinogenicity study using the rat was chosen to assess chronic dietary risk to XDE-729 acid. A NOAEL of 20.3 was chosen based on hyperplasia of the renal pelvic epithelium in females observed at 101 mg/kg/day. This NOAEL is protective of developmental effects, observed in the rat at 526 mg/kg/day (NOAEL = 140 mg/kg/day), and of maternal toxicity in both the rat (LOAEL = 526 mg/kg/day) and rabbit (LOAEL 1094 mg/kg/day).

There was no evidence of carcinogenicity in rat and mouse cancer studies on XDE-729 acid, which is classified as “not likely to be carcinogenic to humans.”

Table 1(b).--Summary of Toxicological Doses and Endpoints for XDE-729 acid for Use
in Human Health Risk Assessment

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute dietary (General population including infants and children and females age 13-49)	No hazard from a single exposure was identified in the available database; therefore, no risk is expected from this exposure scenario.		
Chronic dietary	NOAEL = 20.3	Chronic RfD	Rat two-year dietary chronic

(All populations)	mg/kg/day (females) UF _A = 10x UF _H = 10x FQPA SF = 1x	= 0.20 mg/kg/day cPAD = 0.20 mg/kg/day	toxicity/carcinogenicity study NOAEL = 101/20.3 mg/kg/day [M/F] LOAEL = 404/101 mg/kg/day [M/F] based on increased mortality, altered urinalysis parameters, decreased body weight, increased kidney weights, adrenal zone glomerulosa hypertrophy, increased degeneration and regeneration of renal tubules and kidney stones, and bladder pathology in males; in females, hyperplasia of pelvic epithelium of the kidney.
Cancer (Oral, dermal, inhalation)	Classification: Not likely to be carcinogenic to humans		

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure.

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* In evaluating dietary exposure to halauxifen-methyl and the XDE-729 acid metabolite, EPA considered exposure under the petitioned-for tolerances. EPA assessed dietary exposures to these compounds in food as follows:

i. *Acute exposure.* Quantitative acute dietary exposure and risk assessments are performed for a food-use pesticide, if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1-day or single exposure. No such effects were

identified in the toxicological studies for halauxifen-methyl or XDE-729 acid; therefore, quantitative acute dietary exposure assessments were determined unnecessary.

ii. *Chronic exposure.* In conducting individual chronic dietary exposure assessments for these two compounds, EPA used the food consumption data collected between 2003 and 2008 for USDA's National Health and Nutrition Survey/What We Eat in America (NHANES/WWEIA). As to residue levels in food, EPA used tolerance-level residues and assumed 100 percent of all wheat, barley and triticale acres are treated. No processing factors were used due to the lack of residue concentration in processed commodities. Residue chemistry data indicate that halauxifen-methyl (parent compound) converts to the XDE-729 acid metabolite so quickly in the environment that dietary exposure to halauxifen-methyl is expected to be minimal.

iii. *Cancer.* Based on the data summarized in Unit III.A., EPA has concluded that halauxifen-methyl does not pose a cancer risk to humans at dose levels that do not induce liver toxicity or Cypla1 expression. EPA has also concluded that its XDE-729 acid metabolite does not pose a cancer risk to humans. Therefore, separate dietary exposure assessments for the purpose of assessing cancer risk are determined to be unnecessary.

iv. *Anticipated residue and percent crop treated (PCT) information.* EPA did not use anticipated residue and/or PCT information in the dietary assessment for halauxifen-methyl. Tolerance-level residues and 100% CT were assumed for all food commodities.

2. *Dietary exposure from drinking water.* The Agency used screening-level water exposure models in the dietary exposure analysis and risk assessment for halauxifen-methyl and its metabolites (primarily XDE-729 acid) in drinking water. These simulation models take into account data on the physical, chemical, and fate/transport characteristics of halauxifen-methyl and its metabolites. Further information regarding EPA drinking water models used in pesticide exposure assessment can be found at <http://www.epa.gov/oppefed1/models/water/index.htm>.

Based on the Pesticide Root Zone Model /Exposure Analysis Modeling System (PRZM/EXAMS) and Pesticide Root Zone Model Ground Water (PRZM GW), the estimated drinking water concentrations (EDWCs) of halauxifen-methyl were estimated for chronic exposure in a non-cancer assessment. Based on the Screening Concentration in Groundwater (SCI-GROW) model, the EDWCs of the XDE-729 acid metabolite were estimated for chronic exposure in a non-cancer assessment. Modeled estimates of drinking water concentrations were directly entered into the dietary exposure model. For chronic dietary risk assessment of halauxifen-methyl only, the water concentration value of 0.007 ppb was used to assess the contribution to drinking water. For chronic dietary risk assessment of XDE-729 acid, a drinking water concentration value of 19.5 ppb was used to assess the contribution to drinking water.

3. *From non-dietary exposure.* The term “residential exposure” is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). Halauxifen-methyl is not used, nor is it being proposed for use in any specific use patterns that would result in residential exposure.

4. *Cumulative effects from substances with a common mechanism of toxicity.* Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider “available information” concerning the cumulative effects of a particular pesticide's residues and “other substances that have a common mechanism of toxicity.” EPA has not found halauxifen-methyl or XDE-729 acid to share a common mechanism of toxicity with any other substances, nor do they appear to produce any toxic metabolites produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that neither of these compounds have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which

chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at <http://www.epa.gov/pesticides/cumulative>.

D. Safety Factor for Infants and Children

1. *In general.* Section 408(b)(2)(C) of FFDCA provides that EPA shall apply an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the FQPA Safety Factor (SF). In applying this provision, EPA either retains the default value of 10X, or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor.

2. *Prenatal and postnatal sensitivity.* There was no evidence of increased prenatal susceptibility to either compound and no evidence of postnatal susceptibility to XDE-729 acid. Residual concerns for postnatal susceptibility to halauxifen-methyl in the absence of reproductive toxicity data are low, due to selection of a conservative endpoint and assumptions for dietary exposure, as well as the low level of exposure expected from proposed use patterns.

3. *Conclusion.* EPA has determined that reliable data show the safety of infants and children would be adequately protected if the FQPA SF were reduced to 1x. That decision is based on the following findings:

- i. The toxicity database for halauxifen-methyl and XDE-729 acid are complete.
- ii. There is no indication that halauxifen-methyl or XDE-729 acid are neurotoxic chemicals and there is no need for developmental neurotoxicity studies or additional UFs to account for neurotoxicity.

iii. There is no evidence to suggest that exposure to halauxifen-methyl or XDE-729 acid results in increased *in utero* susceptibility in rats or rabbits in the prenatal developmental studies or in young rats in the 2-generation reproduction study.

iv. There are no residual uncertainties identified in the exposure databases. The chronic dietary food exposure assessment was based on 100 PCT and tolerance-level residues. EPA also made conservative assumptions in the ground and surface water modeling used to assess exposure to halauxifen-methyl and XDE-729 acid in drinking water. These assessments will not underestimate the exposure and risks posed by these compounds.

E. Aggregate Risks and Determination of Safety

EPA determines whether acute and chronic dietary pesticide exposures are safe by comparing aggregate exposure estimates to the acute PAD (aPAD) and chronic PAD (cPAD). For linear cancer risks, EPA calculates the lifetime probability of acquiring cancer given the estimated aggregate exposure. Short-, intermediate-, and chronic-term risks are evaluated by comparing the estimated aggregate food, water, and residential exposure to the appropriate PODs to ensure that an adequate MOE exists.

1. *Acute risk.* An acute aggregate risk assessment takes into account acute exposure estimates from dietary consumption of food and drinking water. No adverse effect resulting from a single oral exposure was identified and no acute dietary endpoint was selected. Therefore, neither halauxifen-methyl, nor XDE-729 acid are expected to pose an acute risk.

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that chronic exposure to halauxifen-methyl from food and water will utilize < 1 % of the cPAD for all infants, the population group receiving the greatest exposure. In addition, EPA has concluded that chronic exposure to XDE-729 acid from drinking water will also utilize < 1 % of the cPAD for all infants. XDE-729 is not a residue of concern in

food; therefore, the chronic assessment was based on drinking water only for this acid metabolite. There are no residential uses for halauxifen-methyl being proposed at this time; therefore chronic aggregate risk reflects only dietary exposure to potential residues in food and drinking water.

3. *Short-term risk.* Short-term risk is assessed based on short-term residential exposure plus chronic dietary exposure. Because there is no short-term residential exposure and chronic dietary exposure has already been assessed under the appropriately protective cPAD (which is at least as protective as the POD used to assess short-term risk), no further assessment of short-term risk is necessary.

4. *Intermediate-term risk.* Intermediate-term risk is assessed based on intermediate-term residential exposure plus chronic dietary exposure. Because there is no intermediate-term residential exposure and chronic dietary exposure has already been assessed under the appropriately protective cPAD, no further assessment of intermediate-term risk is necessary.

5. *Aggregate cancer risk for U.S. population.* Long-term dietary studies conducted with XDE-729 acid in the rat and the mouse showed no evidence of carcinogenicity. Based on the MOA and bridging data on halauxifen-methyl, which allowed identification of a POD for liver cancer, halauxifen-methyl is not expected to pose a cancer risk to humans at dose levels below those that induce liver Cyp1a1 expression. Genotoxicity studies were negative for both compounds.

6. *Determination of safety.* Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to halauxifen-methyl and XDE-729 acid residues.

IV. Other Considerations

A. Analytical Enforcement Methodology

Adequate enforcement methodology (LC-MS/MS) with a limit of quantitation of 0.01 ppm is available to enforce the tolerance expression. The multi-residue method, QuEChERS, is adequate for the determination of both residues of halauxifen-methyl and XDE-729 acid in crop commodities. The method may be requested from: Chief, Analytical Chemistry Branch, Environmental Science Center, 701 Mapes Rd., Ft. Meade, MD 20755-5350; telephone number: (410) 305-2905; email address: *residuemethods@epa.gov*.

B. International Residue Limits

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with international standards whenever possible, consistent with U.S. food safety standards and agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4). The Codex Alimentarius is a joint United Nations Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

No MRLs have been established by Codex for halauxifen-methyl on the commodities affected by this action.

C. Revisions to Petitioned-For Tolerances

As noted in Unit II, the petitioned-for livestock commodity tolerances (milk; fat, meat, meat byproducts of cattle, goat, horse, and sheep) are not being established due to the lack of quantifiable residues in livestock commodities associated with the proposed uses in wheat, barley and triticale. In addition, although the petitioner proposed a tolerance of 0.04 ppm for

wheat, hay, EPA has determined that a tolerance of 0.03 ppm is appropriate. When the petitioner determined the proposed tolerances, the metabolite XDE-729 acid was included as a residue of concern. EPA has subsequently determined that this metabolite is not a residue of concern for tolerance enforcement. Residues of metabolite XDE-729 acid were not quantifiable in any of the residue field trials. Therefore, the values for measuring compliance with these tolerances only include residues of halauxifen-methyl. With the exception of wheat, hay, this revision to the residues of concern for tolerance enforcement had no impact on the plant commodity tolerances.

V. Conclusion

Therefore, tolerances are established for residues of halauxifen-methyl, (methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl) pyridine-2-carboxylate) and its major metabolite, XDE-729 acid, expressed as halauxifen-methyl (parent) equivalents, in or on barley, (grain, hay, straw) and wheat, grain at 0.01 ppm; wheat, forage at 0.50 ppm; wheat, hay at 0.03 ppm; and wheat, straw at 0.015 ppm.

VI. Statutory and Executive Order Reviews

This action establishes tolerances under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled “Regulatory Planning and Review” (58 FR 51735, October 4, 1993). Because this action has been exempted from review under Executive Order 12866, this action is not subject to Executive Order 13211, entitled “Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use” (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled “Protection of Children from Environmental Health Risks and Safety Risks” (62 FR 19885, April 23, 1997). This action does not contain any information collections subject to OMB approval under the Paperwork Reduction

Act (PRA) (44 U.S.C. 3501 *et seq.*), nor does it require any special considerations under Executive Order 12898, entitled “Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations” (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerances in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*), do not apply.

This action directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined that Executive Order 13132, entitled “Federalism” (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled “Consultation and Coordination with Indian Tribal Governments” (65 FR 67249, November 9, 2000) do not apply to this action. In addition, this action does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act (UMRA) (2 U.S.C. 1501 *et seq.*).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act (NTTAA) (15 U.S.C. 272 note).

VII. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a “major rule” as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: July 28, 2016.

Jack E. Housenger,
Director, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180--[AMENDED]

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

2. Add § 180.691 to subpart C to read as follows:

§ 180.691 Halauxifen-methyl; tolerances for residues.

(a) *General.* Tolerances are established for residues of the herbicide, halauxifen-methyl, including its metabolites and degradates, in or on the commodities in the table below.

Compliance with the tolerance levels specified below is to be determined by measuring only halauxifen-methyl (methyl (4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-2-pyridine carboxylate).

Commodity	Parts per million
Barley, grain	0.01
Barley, hay	0.01
Barley, straw	0.01
Wheat, forage	0.50
Wheat, grain	0.01
Wheat, hay	0.03
Wheat, straw	0.015

(b) *Section 18 emergency exemptions.* [Reserved]

(c) *Tolerances with regional registrations.* [Reserved]

(d) *Indirect or inadvertent residues.* [Reserved]

[FR Doc. 2016-19118 Filed: 8/10/2016 8:45 am; Publication Date: 8/11/2016]